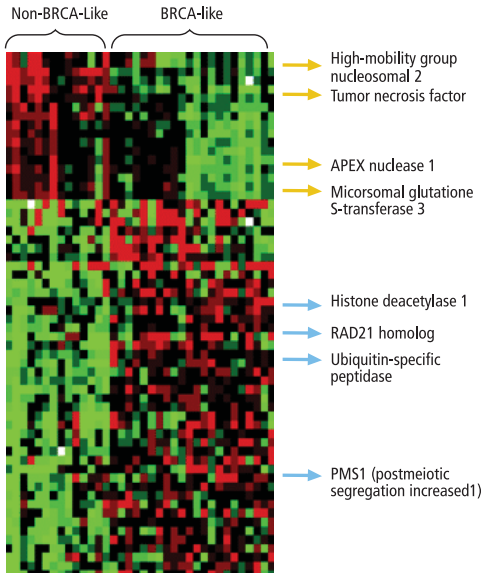
Hematology/Oncology

Lowell E. Schnipper, MD, Chief

Jacalyn Rosenblatt, MD, and David Avigan MD

The mission of the Hematology/Oncology Division is to provide the highest caliber of technologically expert and humane clinical care for men and women with cancer and benign hematological disorders through the combined efforts of superior clinicians, leading-edge scientists, and training programs of unsurpassed excellence. The Division supports an expanding clinical program along with well-funded laboratory, translational and clinical research programs. These serve as a foundation for clinical and research fellowship training, the goal of which is to train today's contributors and tomorrow's leaders, provide delivery of unparalleled clinical care, and generate new knowledge. The Division has 69 faculty members whose diverse clinical, educational and scientific interests are woven into a fabric that makes the whole greater than the sum of its parts.



Expression plot of the 60 genes that comprise the BRCAness profile. The profile is associated with response to platinum and PARP inhibitors and improved survival.

2009–2010 HIGHLIGHTS

Hematological Malignancies and Vaccine Biology Program

The hematological malignancy and hematopoietic stem cell transplantation program provides cutting edge therapies and research for patients with leukemia, lymphoma, multiple myeloma and bone marrow disorders.

Accredited by the Foundation of Cellular Therapy and the National Marrow Donor Program for the performance of autologous and allogeneic transplantation from related or unrelated donors and umbilical cord blood, the program boasts a large multidisciplinary team

David McDermott, MD

The Select Trial – The Biologic Therapy Program at BIDMC has been a leader in the field of cancer immunotherapy for patients with melanoma and kidney cancer. In 2010, the program's Clinical Director, Dr. David McDermott, presented the results of the high-dose IL-2 "Select" Trial. This trial determined that the response rate for HD IL-2 in patients with renal cell carcinoma was significantly better in the modern era than the historical experience, likely as a result of improved patient selection. An improved model for IL-2 patient selection will likely emerge from these efforts and lessons from this work should guide the development of "targeted immunotherapy" (e.g. CTLA-4, PD-1 antibodies) in solid tumors.

of clinicians and scientists. An innovative research focus is the nationally recognized experimental tumor cancer vaccine program. Investigators across Harvard collaborate with Drs. David Avigan and Jacalyn Rosenblatt in the development of a personalized cancer vaccine in which patient-derived tumor cells are fused with dendritic cells (DCs). In a phase I trial of patients with multiple myeloma, vaccination was well tolerated, associated with cellular and humoral anti-tumor immunity and disease stabilization in a majority of patients. In a phase II study, treatment of myeloma patients treated with autologous stem cell transplantation and vaccination resulted in a majority of patients achieving complete remission.

Parallel trials are ongoing in patients with renal, breast and ovarian cancer. The most exciting new development is investigating the impact of vaccination in conjunction with an antibody that reduces immune tolerance, PD-1, in patients with acute myeloid leukemia and multiple myeloma.

PARP Inhibitors in Ovarian Cancer

Obtaining a response to platinum-based chemotherapy is a critical first step in managing patients with epithelial ovarian cancer (EOC). Response to platinum is associated with inability to repair platinum-induced DNA damage, partly due to defects in homologous

SELECTED PUBLICATIONS

Panka DJ, Sullivan RJ, Mier JM. An inexpensive, specific and highly sensitive protocol to detect the BrafV600E mutation in melanoma tumor biopsies and blood. *Melanoma Res* 2010; 20:401-7.

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Choi HS, Liu W, Liu F, Nasr K, Misra P, Bawendi MG, Frangioni JV. Design considerations for tumour-targeted nanoparticles. *Nat Nanotechnol* 2010; 5:42-7.

Lee TH, Lim J, Tun-Kyi A, Finn G, Shi R, Balastik M, Pastorino L, Wulf G, Zhou XZ, Lu KP. Essential role of Pin1 in the regulation of TRF1 stability and telomere maintenance. *Nature Cell Biol* 2009; 11:97-105.

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RESEARCH FUNDING

	Direct	Indirect
Federal	**16,434,675**	**6,143,835**
Non Federal	**8,649,375**	**1,128,847**

recombination (HR). Cells that exhibit defective HR often harbor abnormalities in the BRCA-1/2 pathway and also respond to an exciting new class of agents called PARP inhibitors. The laboratory of Drs. Cannistra and Konstantinopoulos recently identified a 60 gene microarray profile associated with response to platinum and PARP inhibitors, improved survival, and defective HR. This gene expression array, called the "BRCAness" profile, has enabled the investigation of the molecular basis for defective HR in ovarian cancer, regardless of whether the tumor harbors a germline defect in BRCA-1 or -2. The ability to identify defects in HR, even in the presence of wildtype BRCA-1 or -2, is compelling evidence to suggest that other components of the HR pathways are defective in some patients with EOC. The Cannistra/Konstantinopoulos lab is also using this profile to determine its predictive value in the choice of PARP inhibitors in patients with recurrent disease. It is hoped that a better understanding of the HR pathway in ovarian cancer will lead to novel approaches designed to delay or prevent the development of drug resistance in EOC. (*Journal of Clinical Oncology* 2010; 28:3555-3561)

FACULTY

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Xiao Zhou, PhD
Jeff Zwicker, MD

HONORS AND AWARDS

Michael Atkins, MD – Team Science Award, International Society for Biological Therapy of Cancer (2010); Exceptional Service Award, International Society for Biological Therapy of Cancer (2010)

Stephen Cannistra, MD – elected Editor-in-Chief, *Journal of Clinical Oncology*

Stephen Balk, MD, PhD – promoted to Professor of Medicine, Harvard Medical School

Ryan Sullivan, MD – Harvard Skin SPORE Career Development Award (2009)

Ralph Scully, MB, PhD – three new NIH and DoD research grants

Hak Soo-Choi, PhD – Dana Foundation Faculty Development Award, Dana Foundation, NY

John Frangioni, MD, PhD – Visiting Professor of the Royal Netherlands Academy of Arts and Sciences, Amsterdam, The Netherlands

Reed Drews, MD – ASH Medical Education Subcommittee, and the ASH Annual Meeting Planning Subcommittee

Vassiliki Boussiotis, MD, PhD – two new research awards

Daniel Costa, MD, PhD – American Society of Clinical Oncology (ASCO) Career Development Award (CDA)

Akash Patnaik, MD, PhD – AACR-Astellas USA Foundation Fellowship in Clinical/Translational Cancer Research; Clinical Investigator Training Program Fellowship

David McDermott, MD – new appointments: Editorial Board, *Journal of Clinical Oncology*; Director of Cytokine Working Group; ASCO Scientific Program Committee, Melanoma Section; NCI GU Clinical Trial Task Force